Amendments to the claims

1. (currently amended) A method of inhibiting expression of an endogenous cellular gene in a cell, the method comprising the ~~steps~~ step of:

administering to the cell a nucleic acid molecule comprising a polynucleotide sequence which encodes a first engineered zinc finger protein, wherein

(i) said polynucleotide sequence is operably linked to a promoter, ~~and wherein~~

(ii) the nucleic acid molecule expresses the zinc finger protein in the cell; ~~and~~

~~contacting~~

(iii) the zinc finger protein contacts a first target site in the endogenous cellular gene ~~with the zinc finger protein, wherein~~ ; and

(iv) the K_d of the zinc finger protein is less than about 25 nM;

thereby inhibiting expression of the endogenous cellular gene.

2. (previously presented) The method of claim 1, wherein the step of administering further comprises administering a second zinc finger protein-encoding nucleic acid operably linked to a promoter that expresses a second zinc finger protein in the cell, and wherein the step of contacting further comprises contacting a second target site in the endogenous cellular gene with the second zinc finger protein.

3. (original) The method of claim 2, wherein the first and second target sites are adjacent.

4. (previously presented) The method of claim 3, wherein the first and second zinc finger proteins are covalently linked, forming a fusion protein.

5. (original) The method of claim 1, wherein the first zinc finger protein is a fusion protein comprising a regulatory domain.

6. (original) The method of claim 5, wherein the first zinc finger protein is a fusion protein comprising at least two regulatory domains.

7. (original) The method of claim 2, wherein the first and second zinc finger proteins are fusion proteins, each comprising a regulatory domain.

8. (original) The method of claim 7, wherein the first and second zinc finger protein are fusion proteins, each comprising at least two regulatory domains.

9. (currently amended) A method of inhibiting expression of an endogenous cellular gene in a cell, the method comprising the ~~steps~~ step of:

administering to the cell a nucleic acid molecule comprising a polynucleotide sequence which encodes an engineered fusion zinc finger protein, wherein

(i) said polynucleotide sequence is operably linked to a promoter;

[[, wherein]]

(ii) the nucleic acid molecule expresses [[a]] the fusion zinc finger protein in the cell; [[, and wherein]]

(iii) the fusion zinc finger protein comprises six fingers and a regulatory domain; ~~and~~

~~contacting~~ (iv) the fusion zinc finger protein contacts a target site in the endogenous cellular gene ~~with the fusion zinc finger protein, wherein~~ and;

(v) the K_d of the fusion zinc finger protein is less than about 25 nM;

thereby inhibiting expression of the endogenous cellular gene.

10. (original) The method of claim 1, wherein the cell is selected from the group consisting of animal cell, a plant cell, a bacterial cell, a protozoal cell, or a fungal cell.

11. (original) The method of claim 10, wherein the cell is a mammalian cell.

12. (original) The method of claim 11, wherein the cell is a human cell.

13. (original) The method of claim 1, wherein expression of the endogenous cellular gene is inhibited by at least about 75%-100%.

14. (previously presented) The method of claim 1, wherein the endogenous cellular gene is selected from the group consisting of VEGF, ERα, IGF-I, c-myc, c-myb, ICAM, and Her2/Neu.

15. (original) The method of claim 1, wherein the endogenous cellular gene is VEGF.

16. (original) The method of claim 1, wherein the inhibition of gene expression prevents gene activation.

17. (original) The method of claim 5 or claim 7, wherein the regulatory domain is selected from the group consisting of a transcriptional repressor, an endonuclease, a methyl transferase, and a histone deacetylase.

18. (previously presented) The method of claim 1, wherein the step of administering the nucleic acid molecule to the cell comprises administering the nucleic acid molecule in a lipid:nucleic acid complex or as naked nucleic acid.

19. (previously presented) The method of claim 1, wherein the nucleic acid molecule is an expression vector comprising a zinc finger protein-encoding nucleic acid operably linked to a promoter.

20. (previously presented) The method of claim 19, wherein the expression vector is a viral expression vector.

21. (canceled)

22. (previously presented) The method of claim 20, wherein the expression vector is a retroviral expression vector, an adenoviral expression vector, or an AAV expression vector.

23. (previously presented) The method of claim 20, wherein the promoter to which the zinc finger-encoding nucleic acid is operably linked is an inducible promoter.

24. (previously presented) The method of claim 20, wherein the promoter to which the zinc finger-encoding nucleic acid is operably linked is a weak promoter.

25. (original) The method of claim 1, wherein the cell comprises less than about $1.5x10^6$ copies of the zinc finger protein.

26. (original) The method of claim 1, wherein the target site is upstream of a transcription initiation site of the endogenous cellular gene.

27. (original) The method of claim 1, wherein the target site is adjacent to a transcription initiation site of the endogenous cellular gene.

28. (previously presented) The method of claim 1, wherein the target site is adjacent to an RNA polymerase pause site, wherein the RNA polymerase pause site is downstream of a transcription initiation site of the endogenous cellular gene.

29. (original) The method of claim 1, wherein the zinc finger protein comprises an SP-1 backbone.

30. (original) The method of claim 29, wherein the zinc finger protein comprises a regulatory domain and is humanized.

31. (currently amended) A method of activating expression of an endogenous cellular gene in a cell, the method comprising the ~~steps~~ step of:

administering to the cell a nucleic acid molecule comprising a polynucleotide sequence which encodes a first engineered zinc finger protein, wherein

(i) said polynucleotide sequence is operably linked to a promoter, ~~and wherein~~

(ii) the nucleic acid molecule expresses the zinc finger protein in the cell; ~~and~~

~~contacting~~

(iii) the zinc finger protein contacts a first target site in the endogenous cellular gene ~~with the zinc finger protein, wherein~~ ; and

(iv) the K_d of the zinc finger protein is less than about 25 nM;

thereby activating expression of the endogenous cellular gene.

32. (previously presented) The method of claim 31, wherein the step of administering further comprises administering a second zinc finger protein-encoding nucleic acid operably linked to a promoter that expresses a second zinc finger protein in the cell, and wherein the step of contacting further comprises contacting a second target site in the endogenous cellular gene with the second zinc finger protein.

33. (original) The method of claim 32, wherein the first and second target sites are adjacent.

34. (previously presented) The method of claim 33, wherein the first and second zinc finger proteins are covalently linked, forming a fusion protein.

35. (original) The method of claim 31, wherein the first zinc finger protein is a fusion protein comprising a regulatory domain.

36. (original) The method of claim 35, wherein the first zinc finger protein is a fusion protein comprising at least two regulatory domains.

37. (original) The method of claim 32, wherein the first and second zinc finger proteins are fusion proteins, each comprising a regulatory domain.

38. (original) The method of claim 37, wherein the first and second zinc finger protein are fusion proteins, each comprising at least two regulatory domains.

39. (currently amended) A method of activating expression of an endogenous cellular gene in a cell, the method comprising the ~~steps~~ step of:

administering to the cell a nucleic acid molecule comprising a polynucleotide sequence which encodes an engineered fusion zinc finger protein, wherein

(i) said polynucleotide sequence is operably linked to a promoter;

[[, wherein]]

(ii) the nucleic acid molecule expresses [[a]] the fusion zinc finger protein in the cell; [[, and wherein]]

(iii) the fusion zinc finger protein comprises six fingers and a regulatory domain; ~~and~~

~~contacting~~ (iv) the fusion zinc finger protein contacts a target site in the endogenous cellular gene ~~with the fusion zinc finger protein, wherein~~ and;

(v) the K_d of the fusion zinc finger protein is less than about 25 nM;

thereby activating expression of the endogenous cellular gene.

40. (original) The method of claim 31, wherein the cell is selected from the group consisting of animal cell, a plant cell, a bacterial cell, a protozoal cell, or a fungal cell.

41. (original) The method of claim 40, wherein the cell is a mammalian cell.

42. (original) The method of claim 41, wherein the cell is a human cell.

43. (original) The method of claim 31, wherein the endogenous cellular gene is activated to at least about 200-500%.

44. (previously presented) The method of claim 31, wherein the endogenous cellular gene is selected from the group consisting of FAD2-1, EPO, GM-CSF, GDNF, VEGF, and LDL-R.

45. (original) The method of claim 31, wherein the endogenous cellular gene is VEGF.

46. (original) The method of claim 31, wherein the activation of gene expression prevents repression of gene expression.

47. (original) The method of claim 35 or 37, wherein the regulatory domain is selected from the group consisting of a transcriptional activator, or a histone acetyltransferase.

48. (previously presented) The method of claim 31, wherein the step of administering the nucleic acid molecule to the cell comprises administering the nucleic acid molecule in a lipid:nucleic acid complex or as naked nucleic acid.

49. (previously presented) The method of claim 49, wherein the nucleic acid molecule is an expression vector comprising a zinc finger protein-encoding nucleic acid operably linked to a promoter.

50. (previously presented) The method of claim 31, wherein the expression vector is a viral expression vector.

51. (canceled)

52. (previously presented) The method of claim 50, wherein the expression vector is a retroviral expression vector, an adenoviral expression vector, or an AAV expression vector.

53. (previously presented) The method of claim 50, wherein the promoter to which the zinc finger- encoding nucleic acid is operably linked is an inducible promoter.

54. (previously presented) The method of claim 50, wherein the promoter to which the zinc finger- encoding nucleic acid is operably linked is a weak promoter.

55. (original) The method of claim 31, wherein the cell comprises less than about $1.5x10^6$ copies of the zinc finger protein.

56. (original) The method of claim 31, wherein the target site is upstream of a transcription initiation site of the endogenous cellular gene.

57. (original) The method of claim 31, wherein the target site is adjacent to a transcription initiation site of the endogenous cellular gene.

58. (previously presented) The method of claim 31, wherein the target site is adjacent to an RNA polymerase pause site, wherein the RNA polymerase pause site is downstream of a transcription initiation site of the endogenous cellular gene.

59. (currently amended) The method of ~~claim 1~~ claim 31, wherein the zinc finger protein comprises an SP-1 backbone.

60. (currently amended) The method of ~~claim 29~~ claim 59, wherein the zinc finger protein comprises a regulatory domain and is humanized.

61. (currently amended) A method of modulating expression of an endogenous cellular gene in a cell, the method comprising the ~~steps~~ step of:

administering to the cell a nucleic acid molecule comprising a polynucleotide sequence which encodes a first engineered zinc finger protein, wherein

(i) said polynucleotide sequence is operably linked to a promoter, ~~and wherein~~

(ii) the nucleic acid molecule expresses the zinc finger protein in the cell, [[;]] and

~~contacting~~ (iii) the zinc finger protein contacts a first target site in the endogenous cellular gene ~~with the zinc finger protein~~,

thereby modulating expression of the endogenous cellular gene.

62. (previously presented) The method of claim 61, wherein the step of administering further comprises administering a second zinc finger protein-encoding nucleic acid operably linked to a promoter that expresses a second zinc finger protein in the cell, and wherein the step of contacting further comprises contacting a second target site in the endogenous cellular gene with the second zinc finger protein.

63. (original) The method of claim 62, wherein the first and second target sites are adjacent.

64. (previously presented) The method of claim 63, wherein the first and second zinc finger proteins are covalently linked, forming a fusion protein.

65. (original) The method of claim 61, wherein the first zinc finger protein is a fusion protein comprising a regulatory domain.

66. (original) The method of claim 65, wherein the first zinc finger protein is a fusion protein comprising at least two regulatory domains.

67. (original) The method of claim 62, wherein the first and second zinc finger proteins are fusion proteins, each comprising a regulatory domain.

68. (original) The method of claim 67, wherein the first and second zinc finger protein are fusion proteins, each comprising at least two regulatory domains.

69. (currently amended) A method of modulating expression of an endogenous cellular gene in a cell, the method comprising the ~~steps~~ step of:

administering to the cell a nucleic acid molecule comprising a polynucleotide sequence which encodes an engineered fusion zinc finger protein, wherein

(i) said polynucleotide sequence is operably linked to a promoter, ~~wherein~~

(ii) the nucleic acid molecule expresses [[a]] the fusion zinc finger protein in the cell, ~~and wherein~~

(iii) the fusion zinc finger protein comprises six fingers and a regulatory domain, [[;]] and

~~contacting~~ (iv) the fusion zinc finger protein contacts a target site in the endogenous cellular gene ~~with the fusion zinc finger protein~~;

thereby modulating expression of the endogenous cellular gene.

70. (original) The method of claim 61, wherein the cell is selected from the group consisting of animal cell, a plant cell, a bacterial cell, a protozoal cell, or a fungal cell.

71. (original) The method of claim 70, wherein the cell is a mammalian cell.

72. (original) The method of claim 61, wherein the cell is a human cell.

73. (previously presented) The method of claim 61, wherein the endogenous cellular gene is selected from the group consisting of VEGF, ERα, IGF-I, c-myc, c-myb, ICAM, Her2/Neu, FAD2-1, EPO, GM-CSF, GDNF, and LDL-R.

74. (original) The method of claim 61, wherein the endogenous cellular gene is VEGF.

75. (original) The method of claim 65 or claim 67, wherein the regulatory domain is selected from the group consisting of a transcriptional repressor, an endonuclease, a methyl transferase, and a histone deacetylase.

76. (previously presented) The method of claim 61, wherein the step of administering the nucleic acid molecule to the cell comprises administering the nucleic acid molecule in a lipid:nucleic acid complex or as naked nucleic acid.

77. (previously presented) The method of claim 61, wherein the nucleic acid molecule is an expression vector comprising a zinc finger protein-encoding nucleic acid operably linked to a promoter.

78. (previously presented) The method of claim 77, wherein the expression vector is a viral expression vector.

79. (canceled)

80. (previously presented) The method of claim 78, wherein the expression vector is a retroviral expression vector, an adenoviral expression vector, or an AAV expression vector.

81. (previously presented) The method of claim 78, wherein the promoter to which the zinc finger-encoding nucleic acid is operably linked is an inducible promoter.

82. (previously presented) The method of claim 78, wherein the promoter to which the zinc finger-encoding nucleic acid is operably linked is a weak promoter.

83. (original) The method of claim 61, wherein the cell comprises less than about $1.5x10^6$ copies of the zinc finger protein.

84. (original) The method of claim 61, wherein the target site is upstream of a transcription initiation site of the endogenous cellular gene.

85. (original) The method of claim 61, wherein the target site is adjacent to a transcription initiation site of the endogenous cellular gene.

86. (previously presented) The method of claim 61, wherein the target site is adjacent to an RNA polymerase pause site, wherein the RNA polymerase pause site is downstream of a transcription initiation site of the endogenous cellular gene.

87. (original) The method of claim 61, wherein the zinc finger protein comprises an SP-1 backbone.

88. (currently amended) The method of ~~claim 88~~ claim 87, wherein the zinc finger protein comprises a regulatory domain and is humanized.